Chapter 3: Exposure and Dose

3.1 Introduction

To characterize risk assessors compare exposure intakes with toxicity values. Historically, these calculations have relied on divergent definitions of exposure and dose (USEPA, 1986a; 1992a). CERCLA guidance documents have consistently defined exposure as contact with a chemical or physical agent (e.g., USEPA, 1986b, 1989a, 1992a). However, the terminology used in defining the point of contact where exposure takes place is inconsistent and has led to ambiguity in the use of terms and units for estimating the magnitude of exposure. This has resulted in calculational disparities of risk levels. This chapter provides an overview of the evolution and use of the terms exposure and dose, the issues associated with calculating exposure and dose according to these changing definitions, and approaches that DOE assessors could take when engaging regulators in a dialogue on calculating exposure and dose as outlined in EPA guidelines.

3.2 Discussion of Exposure and Dose in Statutes, Regulations, and Guidelines

3.2.1 Statutes and Regulations

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) of 1980, the Superfund Amendments and Reauthorization Act (SARA) of 1986, and the National Oil and Hazardous Substances Pollution Contingency Plan (NCP) of 1985 and its revisions in 1990 (USEPA, 1985a; 1990) are the statutes and regulations that establish the broadly defined goal of reducing and mitigating human exposures to hazardous wastes. The statutes and regulations are implemented by guidelines published in Guidance on Remedial Investigations Under CERCLA (RI) (USEPA, 1985b) and Guidance on Feasibility Studies Under CERCLA (FS) (USEPA, 1985c), later consolidated as Guidance for Conducting Remedial Investigations and Feasibility Studies Under CERCLA (RI/FS) (USEPA, 1988a) to reflect the SARA amendments made to CERCLA in 1986.

CERCLA, SARA, NCP, and the RI/FS documents do not provide specific guidance on how to conduct baseline risk assessments and, as such, do not define exposure or dose. The documents provide general directives regarding risk assessments:

- CERCLA was amended by SARA to "assure, to the maximum extent feasible, that the system accurately assesses the relative degree of risk to human health."

- The NCP of 1985 indicated that CERCLA investigations should consider "the assessment of the population at risk, the routes of exposure, and the amount, concentration, hazardous properties, and environmental fate and transport of the substances present."

- The NCP of 1990 states that exposure assessments be conducted "to identify the magnitude of actual or potential human or environmental exposures, the frequency and duration of those exposures, and the routes by which receptors are exposed."

3.2.2 Guidelines

The risk assessment guidance documents that were developed to support the RI/FS process discuss exposure and dose issues in detail. This section focuses on the evolution of the definition of exposure and dose through these guidelines. Guidance on how to conduct CERCLA risk assessments was initially provided in the Superfund Public Health Evaluation Manual (SPHEM) (USEPA, 1986b). Later, SPHEM was revised and published as Risk Assessment Guidance for Superfund (USEPA, 1989a). In addition to SPHEM and RAGS, EPA developed further guidance supporting CERCLA risk assessments, such as the Superfund Exposure Assessment Manual (SEAM) (USEPA, 1988b), the Exposures Factors Handbook (EFH) (USEPA, 1989b), and exposure assessment guidelines (USEPA, 1986a; 1992a). In between these important guidelines have been other documents in which exposure and dose are addressed. Following is an overview of these EPA documents and guidelines, which are listed in chronological order.

Guidelines for Estimating Exposures

The Federal Register of September 24, 1986, [51 FR 34042] published the final EPA Guidelines for Estimating Exposures, as well as the responses to comments by the public and the EPA Scientific Advisory Board (SAB) on the guidelines. The guidelines, which provide a framework for performing exposure assessments, defined exposure as "the contact with a chemical or physical agent" (USEPA, 1986a). The agency defended this definition as the definition used by the Committee E-47, Biological Effects and Environmental Fate of the American Society for Testing and Materials (ASTM). According to EPA, the magnitude of exposure should be determined by measuring or estimating the amount of an agent at the exchange boundaries (i.e., lungs, gut, skin) during some specified time. EPA also stated in the guidelines that "contact between the subject of concern and the agent may lead to the intake of some of the agent," and that "if absorption occurs, this constitutes an uptake (or an absorbed dose)."

Superfund Public Health Evaluation Manual (SPHEM)

SPHEM provided detailed guidance on how to conduct a public health evaluation at a CERCLA site (USEPA, 1986b). SPHEM indicated that its exposure assessment procedures were the result of earlier draft guidelines which also provided additional scientific background. Exposure assessment is defined in SPHEM as "an estimation of the probable dose of a substance to a target population." Exposure is expressed as "intake," defined as the "amount of substance taken into the body per unit body weight per unit time." Intake is used instead of dose because the information required to estimate dose is often unavailable: "To estimate dose, information indicating the amount of a chemical that may be absorbed (e.g., across lung or GI tract lining or through the skin) and subsequently distributed to target organs or tissues would be needed."

Superfund Exposure Assessment Manual (SEAM)

SEAM (USEPA, 1988b) provided specific methodologies for estimating contaminant release, environmental fate and transport, and human exposure to contaminants emanating from hazardous waste sites. Developed to give consistency in conducting exposure assessments at CERCLA sites within the framework provided by SPHEM, SEAM compiled and integrated a host of medium- and setting-specific techniques published by EPA and others. SEAM was the first document to present a fully integrated body of specific estimation methods that, as a whole, addresses the range of possible exposure settings that may need to be evaluated at an uncontrolled hazardous waste site.

SEAM defines exposure as "the amount of pollutant contacting body boundaries (skin, lungs, or intestinal tract)." Estimates of exposure are expressed in mass of contaminant per unit of body mass per day.

The Exposure Factors Handbook (EFH)

The EPA's guidelines for estimating exposures, as delineated in SEAM, were expanded and improved in the Exposure Factors Handbook (USEPA, 1989b). The handbook, intended to serve as a support document to the 1986 EPA's Guidelines for Estimating Exposures, provides basic equations for estimating exposure for various exposure scenarios. Exposure is defined in EFH as "the contact with a chemical or physical agent." The magnitude of the exposure is calculated as "the amount of the agent available at human exchange boundaries (skin, lungs, gut) during some specified time."

EFH indicates that exposure may also be referred to as "administered dose." Since the dose/response curve is derived from animal toxicological studies on the basis of the administered dose, EFH recommends that exposure should be expressed on a comparable basis.

EPA Region I Supplemental Guidance

EPA Region I (Connecticut Maine, Massachusetts, New Hampshire, Rhode Island, Vermont) released the Region I Supplemental Manual to Risk Assessment Guidance for the Superfund Program (USEPA, 1989c). EPA Region I guidance differentiates "exposure point concentration," which is "the amount of chemical in an environmental medium to which one may be exposed and "exposure dose," which is "a term used to describe the resulting exposure from a particular concentration." Exposure dose was also noted in the EPA Region I guidance as being "similar to the administered dose of a laboratory experiment from which cancer potency factors and reference doses are usually derived."

Risk Assessment Guidance for Superfund, Volume I (RAGS)

RAGS (USEPA, 1989a) constitutes the present conceptual framework for CERCLA risk assessments. The exposure assessment process and the quantification of exposures is delineated in RAGS as follows "The exposure assessor calculates chemical-specific exposures for each exposure pathway. Exposure estimates are expressed in terms of the mass of substance in contact with the body per unit body

weight per unit time. These exposure estimates are termed intakes and represent the normalized exposure rate (equivalent to intake)."

RAGS contains several definitions associated with exposure and dose. Following is a list of these definitions.

- Absorbed Dose: The amount of a substance crossing the exchange boundaries (e.g., gut, lung, skin) after contact. It is calculated from the intake and the absorption efficiency for that particular chemical. The absorbed dose is equivalent to intake' multiplied by the absorption factor.

- Administer d Dose: The mass of a substance purposely given to a test organism that is in contact with an exchange boundary (e.g., gut) per unit body weight per unit time. Administered dose is equivalent to intake.

- Applied Dose: The amount of a substance purposely given to a test organism for dermal toxicity experiments.

- Exposure: Contact of an organism with a chemical or physical agent at the exchange boundaries of the organism (e.g., skin, lungs, gut) and available for absorption. It is quantified as the amount of substance at the exchange boundary.

- Intake: This is termed the normalized exposure rate, and is expressed as the mass of a substance in contact with the exchange boundary per unit body weight per unit time (e.g., mg chemical per kg body weight per day). It is also equivalent to administered and applied dose.

Exposure Assessment Methods Handbook (EAMH)

The Exposure Assessment Methods Handbook (USEPA, 1991) was published to provide guidance to exposure assessors on methodologies to estimate concentrations of chemicals in the environment. EAMH also provides an overview of the exposure assessment process, where it defines exposure and dose in a manner consistent with the EFH. Both documents abide by the definitions set forth in the 1986 exposure guidelines, where exposure is defined as "contact with a chemical or physical agent," and the magnitude of exposure is defined as "the amount available at the exchange boundaries (skin, lungs, gut)" (USEPA, 1986a).

EAMH equates the term "exposure" with the term "administered dose": "For most exposure assessments, the dose is estimated based on external exposure because the human/animal toxicological data used in combination with exposure data to calculate risk are most frequently based on administered dose or ambient exposure rather than internal dose." However, the EAMH recommends that when calculating exposure estimates incurred from different exposure routes, "the absorbed dose is the desired common denominator for different routes." EAMH refers to absorbed dose as "a function of the degree of

penetration through and chemical transfer across barriers (e.g., skin) and membranes (e.g., the lining of the lung) that the chemical contacts."

Dermal Exposure Assessment: Principles and Applications (DEAPA)

Dermal Exposure Assessment: Principles and Applications (USEPA, 1992b) addressed the quantification of human risks due to dermal exposures. This document defines exposure as "the contact between a contaminant and the external boundary of an organism." However, this document states that dermal exposure assessments are defined as "including the estimation of absorbed doses from contaminants contacting the skin."

DEAPA indicates that dose estimates are needed in dermal exposure assessments because 'oral dose-response relationships and toxicity reference values are based on the "potential (i.e., administered) dose," whereas the dermal dose estimates are based on the absorbed dose. This document also remarks that the cancer slope factors and RfDs used in CERCLA risk assessments are based on toxicological studies of ingestion or inhalation exposure, not dermal exposure.

Guidelines for Exposure Assessment

These guidelines (USEPA, 1992a), published in response to recommendations from EPA's SAB and the general public, superseded and replaced the Guidelines for Estimating Exposures (USEPA, 1986a) and Proposed Guidelines for Exposure-Related Measurements (USEPA, 1988c). The guidelines convey the principles of exposure assessments and constitute the current theoretical framework to be used in the Superfund program. The goal of the document is to outline a method of calculating human exposures to contaminants from hazardous waste sites that is "a more realistic approach to exposure determination."

EPA acknowledged that the terminology in previous exposure guidelines raised concerns regarding inconsistencies in defining the point at which exposure occurs on the body. As a result of the review by the public and SAB, EPA revised both the definition and usage of these terms in order to&in accordance with definitions "suggested by the National Academy of Sciences. " Definitions of the following terms are included in the document:

- Exposure: Contact of a chemical, physical, or biological agent with the outer boundary of an organism. Exposure is quantified as the concentration of the agent in the medium in contact with the organism integrated over the time duration of the contact. Exposure is calculated using monitoring data and models.

- Dose: The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism. Administered Dose is the amount of a substance given to a test subject (human or animal) through ingestion or inhalation to determine dose-response relationships. In exposure assessment. because exposure to chemicals is usually inadvertent, this quantity is called potential dose. Potential Dose is the amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin. Applied Dose is the amount of a

substance in contact with the primary absorption boundaries of an organism (e.g., skin, lung, gastrointestinal tract) and available for absorption (although not necessarily having yet crossed the outer boundary of the organism). Absorbed Dose is the amount of a substance crossing a specific absorption barrier (e.g., the exchange boundaries of the skin, lung, and digestive tract) through uptake processes. Internal Dose is the amount of a substance penetrating across the absorption barriers (the exchange boundaries) of an organism, via either physical or biological processes, without respect to specific absorption barriers or exchange boundaries. This term is synonymous with absorbed dose. 'he amount of the chemical available for interaction by any particular organ or cell is termed the Delivered Dose for that organ or cell. The administered, potential, and applied doses incorporate intake rate into their values for oral and inhalation exposures. Dermal doses are calculated differently as explained in Section 3.3.2.

3.3 Issues and Regulator Dialogue

3.3.1 Exposure/Dose Issues

Because of the uncertainties inherent to the sciences supporting the risk assessment process, the relationship between exposure and dose is sometimes unclear. The following issues are illustrative.

Semantic Ambiguities in Exposure/Dose Terminology

Review of CERCLA guidance documents revealed that exposure has always been defined in CERCLA exposure assessments as contact with the chemical or agent (e.g., USEPA, 1986a, 1989a, 1992a). However, the terminology used in defining the point of contact where exposure takes place is inconsistent and has led to ambiguity in the use of terms and units for estimating the magnitude of exposure. Specifically y, exposure can be conceptualized as occurring:

Scheme (l): at the exchange boundaries (skin, lungs, gastrointestinal tract), or

Scheme (2): at the visible exterior of a person (skin, mouth, nostrils).

If an exposure assessor follows Scheme (1), ingestion of water is considered an exposure under the old definition; following Scheme (2), that same water ingestion is considered an exposure under the current definition. The choice of either scheme implies that different units be used under the old definition exposure is expressed as the mass of the chemical times the intake rate (e.g., milligrams of chemical/liters of water x liters of water ingested/day x days exposed); under the present definition, exposure is expressed as a concentration of chemical per unit of time (e.g., milligrams of chemical/liters of water x minutes of contact), The old definition of exposure, Scheme (1), is now considered to equate with administered, potential, and applied dose.

The exposure assessment guidelines published in 1992 changed EPA's definition of exposure from "contact with the exchange boundaries (skin, lungs, gastrointestinal tract)" to "contact with the visible exterior of a person (skin, mouth, nostrils)" (USEPA, 1992a). EPA decided to define exposure as contact

with the visible exterior of the person based on comments received from the general public and the scientific community on previous guidelines. The chosen definition is in contrast with the previous view of exposure as "contact with exchange boundaries where contaminants are actually absorbed (skin, lungs, gastrointestinal tract)" (USEPA, 1986a).

Inconsistent Exposure/Dose Calculations

Inconsistencies in conceptualizing exposure and dose are not just restricted to semantic ambiguities; they are intrinsic to how exposure and dose are calculated According to the 1992 exposure assessment guidelines, defining exposure as contact with the visible exterior improves consistence y in quantitative risk assessments. The toxicity values are often derived from dose-response relationships generated in toxicological studies where the chemical under study is administered to animals. That is, toxicity values incorporate intake rate into the value. According to USEPA (1992a) "estimates of doses should be expressed in a manner that can be compared with available dose-response data." The comparison can be made for oral and inhalation exposures after the exposures have been adjusted by the intake rate for that chemical. This adjustment by intake rate is the calculation used to convert oral and inhalation exposures to potential or applied doses. Skin exposure comparisons are discussed in the next section. RAGS recommends the following consistency checks:

1. Averaging period of exposure: Estimated exposure duration should be similar to duration of the toxicological study from which a chemical-specific risk value is derived (i.e., use of subchronic toxicity values to evaluate short-term exposures).

2. Exposure route: Toxicity values used for each pathway should be consistent with exposure route (e.g., oral toxicity values should be consistent with ingestion, inhalation values with respiratory exposures, etc.).

3. Absorption adjustments: Toxicity values and exposure estimates should be expressed as either absorbed doses or as exposure intakes. Except for dermal exposures, exposures are expressed as intakes.

The EPA IRIS database contains the currently available toxicological values to be used in CERCLA risk assessments. Because the IRIS database lacks comprehensive toxicological information for various chemicals (or mixtures of chemicals), often the risk characterization cannot follow the three consistency checks delineated in RAGS. For example, regarding the first check, less-than-lifetime exposures are converted to equivalent lifetime exposures for cancer risk, and chronic RfDs are used in the absence of short-term toxicity values. In relation to the second check, in the absence of inhalation toxicity values the recommendation is to extrapolate from oral toxicity values. Regarding the final check many oral RfDs and slope factors assume ingestion in water, even when toxicity values were derived from studies employing administration in oil by gavage or in feed. Most CERCLA risk assessments encounter various toxicological data gaps requiring extrapolations that may result in inconsistent calculations of dose or exposure.

3.3.2 Regulator Dialogue

EPA has acknowledged that the terms "exposure" and "dose" were defined inconsistent y in various agency documents and guidelines. This raised concerns regarding inconsistencies in defining the point at which exposure occurs on the body (USEPA 1992a). The current acceptable terminology in CERCLA risk assessments is delineated in Guidelines for Exposure Assessment (USEPA 1992a):

- Dose: The amount of a substance available for interaction with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism.

- Exposure: Contact of a chemical, physical, or biological agent with the outer boundary of an organism.

As explained above, intake rates are used to calculate potential or applied doses for inhalation or oral exposures, The risk assessor uses professional judgement to determine which intake rates to use in calculating doses. Any intake rate can be negotiated so long as it can clearly be defended as appropriate for use at that site. Some default intake rates used are overly conservative. For example, the drinking water intake rate of 2 L/day is based on the U.S. Army rate for soldiers in the field. This scenario is generally not applicable for Superfund sites. EFH (USEPA, 1989b) states "the Agency believes that a water consumption rate of 2 L per day is an overestimate for most people."

Exposures are estimated using monitoring data and models. The choice of models, and the variables used in the models are determined by the risk assessor. As with intake rates, any model or variable can be negotiated with EPA so long as it can clearly be defended as appropriate for use at that site. The models given in EPA guidance documents are examples of models that can be used, but the risk assessor is not required to use those particular models and/or model variables. EAMH (USEPA, 1991) states that the document "should help improve the consistency with which exposure assessments are conducted across the Agency, but still allow different approaches that may be appropriate based on considerations of policy, precedent, or other factors." The effect that conservative default values have on the risk assessment is discussed in detail in Chapter 9.

The chemicals of concern in CERCLA sites are usually contained in air, ground water, surface water, soils, and/or sediments. Exposure concentration is calculated as the concentration of the chemical of concern at the point of contact, over a period of time. The guidelines suggest meaningful comparisons between exposure calculations and toxicological values. But while the advice for consistent comparisons is warranted as a precautionary matter, the limitations of the available toxicity data can still hinder the characterization of risk. For example, dermal risk levels in CERCLA risk assessments frequently are calculated using oral-derived toxicity values because the reference doses derived from dermal exposure experiments are often unavailable. The resulting trans-pathway calculation introduces additional uncertain y into the risk assessment.

To calculate an exposure intake and compare it to toxicity values, exposure assessors use the term "potential dose," which is defined as the amount of the chemical ingested, inhaled, or applied to the skin (USEPA, 1992b). Although potential dose simplifies the conceptualization of dose, there are implications

to its use, particularly in dermal exposures where absorption is an uptake across the outer boundary. Potential dose in dermal exposures includes the amount of the chemical in the total amount of the medium contacting the skin. This differs from applied dose, which is the amount of the chemical in the layer actually touching the skin. The exposure guidelines warn that calculations of potential or applied dose may not be useful where there is immersion in a fluid such as water.

Consider two dermal exposure (immersion) situations in which the subject is exposed to contaminated surface water. In the first scenario, the subject is exposed while taking a bath in water obtained from a contaminated river. In this case, the assessor may conservatively assume that the individual may be exposed to all of the mass of contaminant in the tub full of bath water, and both the contaminant concentration as well as the total amount of water potentially contacting the body (i.e., the total number of gallons in the tub) can be quantified with confidence. In the second scenario, however, the subject is exposed while swimming in a lake. Although the contaminant concentration is the same in both cases, the maximum amount of water to which the individual may be exposed while swimming is unknown. It seems logical to assume that the swimmer is exposed to a constantly replaced film of contaminated water, but the total mass of the contaminant available for exposure cannot be defined as the total mass of the contaminant in the lake because it is unlikely that the swimmer would contact all the contaminant in the lake.

The problem cited above traditional y was resolved by defining exposure differently for the two scenarios. In the first case, the assessor would conservatively assume that the total mass of contaminant in the bath water is available for exposure, and calculate the magnitude of exposure as a potential dose, (i.e., as a function of contaminant concentration and amount of water applied to the skin). In the second case, the scenario cannot be described as a potential dose (because the swimmer did not contact all the contaminant in the lake), or as an applied dose (because the boundary layer is being constantly renewed). Instead, the scenario is conceptualized as a flux of a contaminant across the skin. Thus, exposure became a function not of concentration and water mass, but of concentration and exposure time. That approach frequently was frustrated by a lack of chemical-specific absorption factors, however, and the absorption rate of pure water was often used as a default value.

The calculation of dermal exposures differs from oral and respiratory exposures because the skin is considered both an exchange boundary and an outer boundary. As indicated in the hypothetical situations described above, the calculation of risks from dermal exposures is dependent on how the exposure scenarios are crafted. When addressing dermal exposure routes, Dermal Exposure Assessment: Principles and Applications (USEPA, 1992a) should be consulted as it contains information pertinent to developing exposure scenarios, and recent information on chemical-specific absorption factors Overly conservative default absorption factors, such as 50 percent or 100 percent, should not be used in BRAs unless it is shown that the chemical in question actually is absorbed at such high rates.

3.4 References

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